Claim Listing

Amendments to the Claims:

This listing of claims will replace all prior version, and listings, of claim in the application:

1. -128. (canceled).

129. (Currently Amended) A method of identifying a compound of interest in a library of compounds, each of said compounds being bound to a solid support and being produced by a unique reaction series composed of N reaction steps, wherein N is an integer of at least 2, and wherein each compound is produced from components which are independently the same or different, the method comprising:

(a) dividing a population of solid support into M batches, wherein M is an integer greater than 1;

(b) reacting each of the M batches of solid support with a component, so that the component forms a bond with the solid support;

(c) adding to one or more batches, prior to (b), concurrently with (b), or subsequently to (b), one or more tag(s), each tag able to be attached to the solid support and able to bo identified by optical interrogation, wherein said one or more tag(s) constitutes a code, which code is uniquely associated with a compound and a corresponding reaction sequence and is determined by optical interrogation;

(d) recombining all of said M batches after (b) and (c);

(e) repeating (a) to (d) for N-1 times, or repeating (a) to (d) for N-2 times followed by repeating (a) to (c) once, to produce a library of compounds;

(f) performing an assay capable of indicating that any compound in the library has a property of interest; and

(g) decoding the code composed of one or more tag(s) by in-situ optical interrogation of the tag(s) to provide the chemical identity of [identify] the compound associated with the code, wherein the decoding step is carried out without isolating the solid support comprising the compound having the property of interest from the other solid supports and without detaching any of the tag(s) from the solid support comprising the compound having the property of interest [and wherein said decoding step comprises in-situ optical interrogation of the tag(s)].

130. (previously presented) The method of claim 160 wherein the solid support comprises a bead.

131. (previously presented) The method of claim 160 wherein (c) comprises repeating (a) to (d) for N-1 times to produce a library of compounds.

132. (previously presented) The method of claim 160, wherein (e) comprises repeating (a) to (d) N-2 times followed by repeating (a) to (c) once to produce a library of compounds.

133. (previously presented) The method of claim 132, further recombining said M batches subsequent to contacting the library of compounds with the target biomolecule.

134. (previously presented) The method of claim 160, wherein each fluorophore tag is in substoichiometric amount compared to the component added in (b).

135. (previously presented) The method of claim 160, wherein each fluorophore tag added in (c) is from about 0.001 to about 0.1 molar equivalent to the component added in (b).

136. (previously presented) The method of claim 160, wherein the optical interrogation of each fluorophore tag comprises determining its relative abundance.

137. (previously presented) The method of claims 160, wherein each fluorophore tag is attached to the solid support by covalent bonding.

138. (previously presented) The method of claim 160, wherein the fluorophore tag is capable of forming a bond to the solid support directly or to the component attached to said solid support.

139. (previously presented) The method of claim 160, wherein the fluorophore tag is a dye selected from the group consisting of compounds with the following chemical structures:

3-(ε-carboxypentyl)-3'-ethyl-oxacarbocyanine-6,6'-disulfonic acid,

1-(ε-carboxypentyl)-1'-ethyl-3,3,3',3'-tetramethylindocarbocyanine-5,5'-disulfonic acid,

1-(ε-carboxypentyl)-1'-ethyl-3,3,3'3'-tetramethyl-3H-benz(e)indocarbocyanine-5,5',7,7'-tetrasulfonic acid, and

1-(ε-carboxypentyl)-1'-ethyl-3,3,3',3'-tetramethylindocarbocyanine-5,5'-disulfonic acid,

and is activated as an active ester selected from the group consisting of succinimidyl, sulfosuccinimidyl, p-nitrophenol, pentafluorophenol, HOBt and N-hydroxypiperidyl.

140. (previously presented) The method of claim 160, wherein the fluorophore tag is a dye selected from the group consisting of compounds with the following chemical structures:

6-((4,4-difluoro-5,7-dimethyl-4-bora-3a,4a-diaza-s-indacene-3-propionyl)amino) hexanoic acid,

6-((4,4-difluoro-5-phenyl-4-bora-3a,4a-diaza-s-indacene-3-propionyl)amino) hexanoic acid,

6-((4,4-difluoro-1,3-dimethyl-5-(4-methoxyphenyl)-4-bora-3a,4a-diaza-s-indacene- 2- propionyl) amino)hexanoic acid,

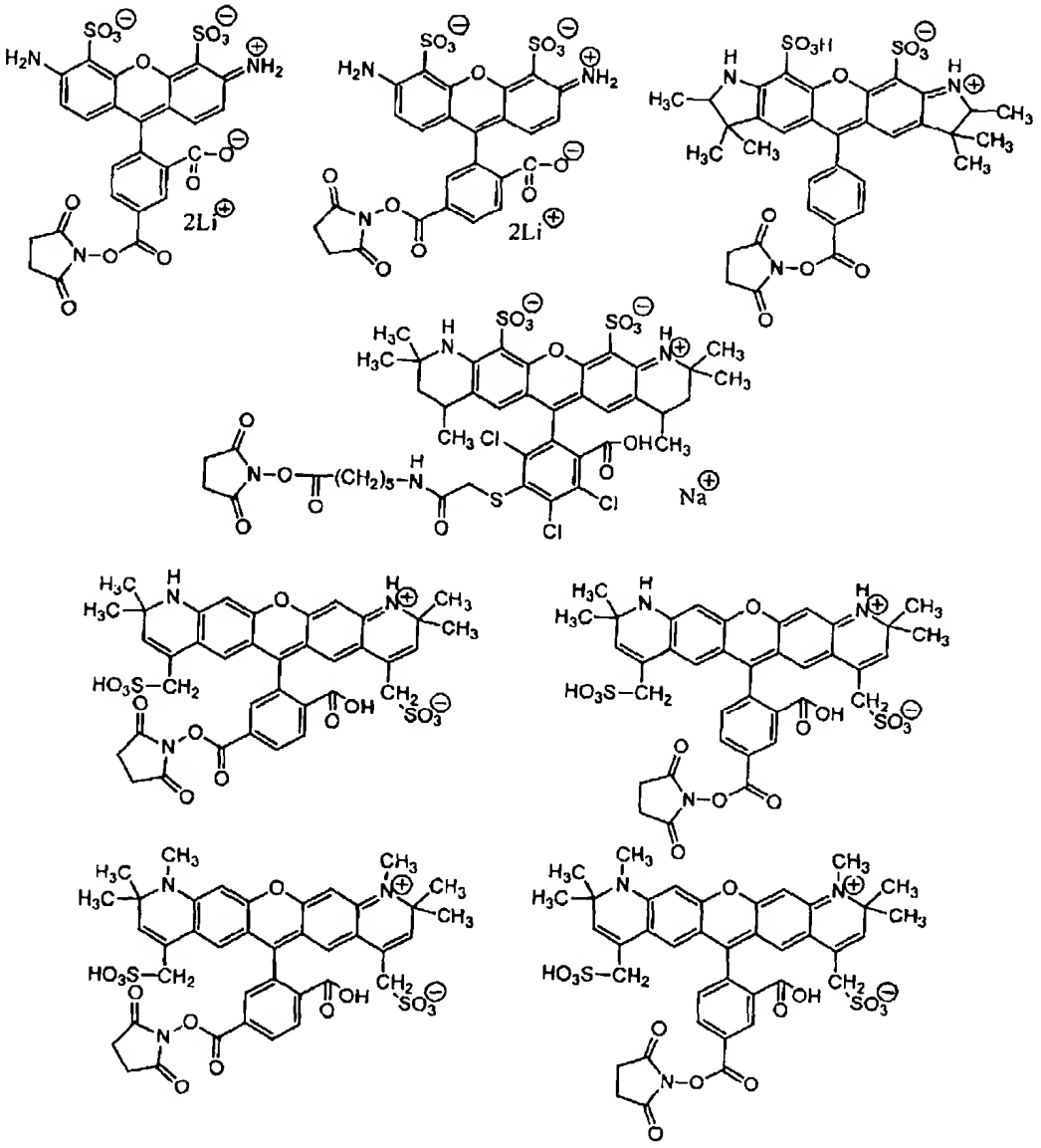
6-(((4-(4,4-difluoro-5-(2-thienyl)-4-bora-3a,4a-diaza-s-indacene-3-yl)phenoxy) acetyl) amino)hexanoic acid,

6-(((4,4-difluoro-5-(2-thienyl)-4-bora-3a,4a-diaza-s-indacene-3-yl)styryloxy)acetyl) aminohexanoic acid, and

6-(((4,4-difluoro-5-(2-pyrrolyl)-4-bora-3a,4a-diaza-s-indacene-3-yl)styryloxy) acetyl)aminohexanoic acid,

and is activated as an active ester selected from the group consisting of succinimidyl, sulfosuccinimidyl, p-nitrophenol, pentafluorophenol, HOBt and N-hydroxypiperidyl.

141. (previously presented) The method of claim 160, wherein the fluorophore tag is a dye selected from the group consisting of compounds with the following chemical structures:



142. (previously presented) The method of claim 160, wherein (g) is carried out using multi-color fluorescence imaging or spectral imaging analysis.

143. (previously presented) The method of claim 160, wherein the decoding is carried using multi-color fluorescence imaging in combination with spectral analysis.

144. (previously presented) The method of claim 160, wherein M is an integer from at least 2 to 25.

145. (previously presented) The method of claim 160, wherein the component is protected or unprotected at a group which is capable of participating in a further coupling reaction and orthogonally protected at non-participating group(s), and wherein (d) further comprises cleaving any protecting group of the component which is to participate in a further coupling reaction.

146. (previously presented) The method of claim 160, wherein the fluorophore tag is optically distinguishable by emission wavelength.

147. (previously presented) The method of claim 160,wherein the fluorophore tag is optically distinguishable by emission intensity by adjusting the ratio of the relative quantities of the fluorophore tags.

148. (previously presented) The method of claim 147, wherein the ratio is from about 1:1 to 4:1.

149. (previously presented) The method of claim 160, wherein the fluorophore tag is optically distinguishable by excited-state lifetime.

150. (previously presented) The method of claim 160, wherein the fluorophore tag is optically distinguishable by emission wavelength, excited-state lifetime and emission intensity.

151. (previously presented) The method of claim 160, wherein the compound of interest comprises an oligonucleotide or nucleic acid.

152. (withdrawn) The method of claim 129, wherein the compound of interest comprises an oligopeptide or a protein.

153. (withdrawn) The method of claim 129, wherein the compound of interest comprises a ligand.

154. (previously presented) The method of claim 160, wherein N is an integer from at least 4 to about 12.

155. (previously presented) The method of claim 130, wherein the decoding is carried out while the beads are on a planar substrate.

156. (previously presented) The method of claim 155 wherein the optical interrogation is carried out using multi-color fluorescent imaging in combination with spectral analysis.

157. (previously presented) The method of claim 130, wherein the decoding is carried out while the beads are arranged in a planar bead array.

158. (previously presented) The method of claim 157 wherein the optical interrogation is carried out using multi-color fluorescent imaging in combination with spectral analysis

159. (previously presented) The method of claim 130, wherein the bead is composed of a material selected from the group consisting of polystyrene, polyethylene, cellulose, polyacrylate, polyacrylamide, silica and glass.

160. (previously presented) The method of claim 129, wherein the tag in (c) comprises a fluorophore tag.

161. (previously presented) The method of claim 129 wherein the tag in (c) comprises a chromophore tag.

162. (previously presented) The method of claim 129 wherein the code is a binary code, an extended binary code, or a simple code.

163. (previously presented) The method of claim 147, wherein a difference in emission intensity is the result of a difference in the ratio of relative quantities of fluorophore tags.

164. (previously presented) The method of claim 129, wherein the property of interest is a binding affinity of a compound to a receptor, the assay is performed by determining a physical response to binding by:

(a) first admixing with the library of compounds a solution of a labeled receptor so as to result in labeled receptor bound to at least one compound bound to a solid support;

(b) removing the solution from the solid support;

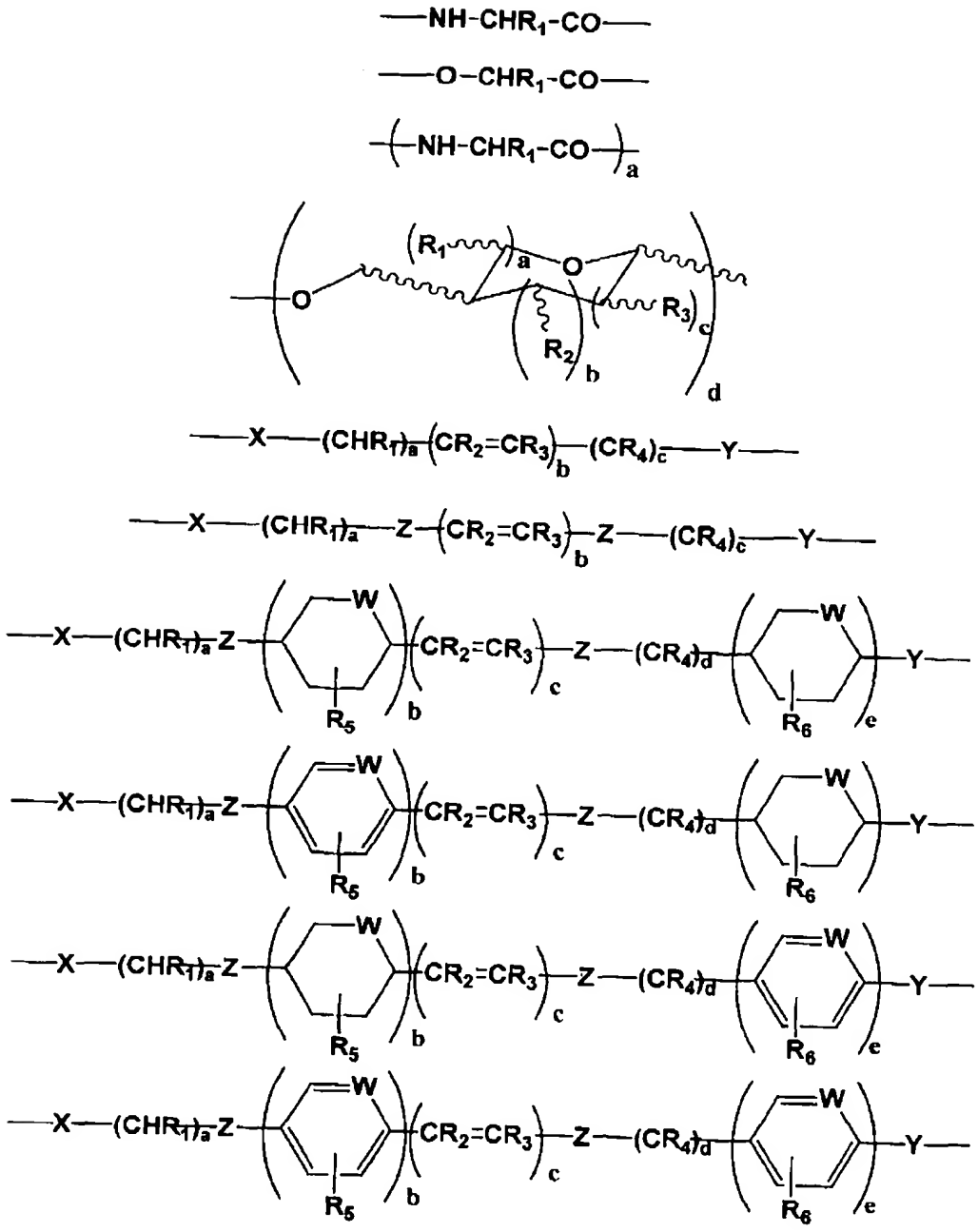
(c) optionally washing the solid support so as to substantially remove non-bound labeled receptor; and

(d) measuring the physical response due to bound labeled receptor so as to determine the binding affinity.

165. (previously presented) The method of claim 164, wherein the receptor is labeled by a fluorescent dye, a colored dye, a radioisotope or an enzyme.

166. (previously presented) The method of claim 164, wherein the physical response is fluorescence emission, optical absorption or radioactivity.

167. (withdrawn) The method of claim 129, wherein the components have a structure independently selected from the group consisting of:



wherein R_1, R_2, R_3, R_4, R_5 and R_6 are independently methyl, ethyl, linear or branched chain C_3-C_9, phenyl, benzoyl, cyano, nitro, halo, formyl,

acetyl and linear or branched chain C_3-C_9 acyl; wherein a, b, c, d and e are independently 0, 1, 2 or 3; wherein X, Y and Z are independently NH, O, S, S(=O), CO, (CO)O, O(CO), NH(C=O) or (C=O)NH; and wherein W is independently N, O or S.

168. (previously presented) The method of claim 129, wherein the assay is performed by cleaving compounds from the solid support while permitting diffusion through solution and binding to receptors, said receptors arranged in proximity to each solid support.

169. (previously presented) The method of claim 129, wherein the decoding step comprises the steps of:

(a) collecting spectral fluorescence data for each respective solid support so as to determine the respective abundance of the tag(s) bound thereto; and

(b) analyzing the collected spectral fluorescence data by comparing the respective relative abundances of the tag(s) determined in (a) so as to determine the unique reaction series for the component, thereby identifying the compound having the property of interest.

170. (previously presented) The method of claim 169 wherein the solid support is a bead.

171. (previously presented) The method of claim 170 wherein spectral fluorescence data is collected by:

(a) forming a static planar array or a dynamic planar array of beads; and

(b) obtaining a fluorescence image for each bead.

172. (previously presented) The method of claim 171, wherein the planar array of beads is formed adjacent to the planar walls of a sandwich flow cell and controlled by light-controlled electrokinetic means.

173. (previously presented) The method of claim 170, wherein spectral fluorescence data are collected for the bead array by initially forming a spatially encoded array of beads at an interface between an electrode and an electrolyte solution, comprising the following steps:

(a) providing an electrode and an electrolyte solution;

(b) providing multiple types of beads, each type being stored in accordance with chemically or physically distinguishable bead characteristics in one of a plurality of reservoirs, each reservoir containing a plurality of like-type beads suspended in said electrolyte solution;

(c) providing said reservoirs in the form of an *mxn* grid arrangement;

(d) patterning said electrode to define *mxn* compartments corresponding to said *mxn* grid of reservoirs;

(e) depositing *mxn* droplets from said *mxn* reservoirs onto said corresponding *mxn* compartments, each said droplet originating from one of said reservoirs and remaining confined to one of said *mxn* compartments and each said droplet containing at least one bead;

(f) positioning a top electrode above said droplets so as to simultaneously contact each said droplet;

(g) generating an electric field between said top electrode and said *mxn* droplets;

(h) using said electric field to form a bead array in each said *mxn* compartments, each said bead array remaining spatially confined to one of said *mxn* droplets;

(i) illuminating said *mxn* compartments on said patterned electrode with a predetermined light pattern to maintain the position of said bead arrays in accordance with said predetermined light pattern and the pattern of *mxn* compartments; and

(j) positioning said top electrode closer to said lectrode thereby fusing said *mxn* droplets into a continuous liquid

phase, while maintaining each of said *mxn* bead arrays in one of the corresponding *mxn* compartments.

174. (previously presented) The method of claim 173, wherein said compartments are hydrophilic and the remainder of said electrode surface is hydrophobic.